RECRUITING A PATIENT INTO A CLINICAL TRIAL

Cross Reference to Related Application

This application claims the benefit of priority from U.S. Provisional Patent Application Serial No. 60/227,484, filed August 24, 2000, the entire disclosure of which is incorporated herein by reference.

Background

Drug development is a slow and expensive process, with the ultimate step of clinical trials representing one of the costliest and riskiest steps. For a drug to be approved in most countries, particularly the United States, it must pass through a rigorous process of human testing to determine dosage, adverse effects, and efficacy. Only one in ten drugs which commence clinical trials in the U.S. eventually receive approval for human use. The annual cost of conducting clinical trials in the United States is more than 7.4 billion dollars, representing nearly 33% of all R&D expenditures.

One of the slowest and riskiest steps in the clinical trial process itself is the initial enrollment (or recruitment) of patients in the trial. There are approximately 1,000 drugs in Phase II/III trials in the US at any given time, with 1,400 worldwide. Recruitment in clinical trials takes an average of 40 weeks to complete, with 40-50% of the patients screened ultimately deemed inappropriate. It has been estimated that the number of patients needed for clinical trials is doubling every 5 years. Recent drug discovery technologies such as genomics, combinatorial chemistry, and high throughput screening will tend to exacerbate such a need. In a trial, patients must be matched against strict enrollment parameters to ensure proper evaluation of clinical endpoints in the correct patient population. Patients who are inappropriately enrolled for a particular clinical trial present two problems: an improper skewing of adverse effects, dosage, and efficacy; and a slowing of the clinical trial process itself since more patients must be enrolled as the inappropriate patients are ultimately weeded out.

While the Internet and the World Wide Web can facilitate the rapid and global exchange of vast amounts of information, the very nature of such a networked system implicates security concerns, particularly when sensitive information such as patient health records or proprietary drug trial information could be compromised. Nevertheless, the increased availability of medical information on the Internet has resulted in a public eager to try cutting-edge therapies when traditional methods have failed or when no therapy has been approved, as witnessed by the plethora of web sites related to AIDS and cancer information. However, current methods for clinical trial recruitment, including Internet sites dedicated to providing some clinical trial information, have been inefficient. The FDA Modernization Act of 1997 requires pharmaceutical companies to submit trial information to a national registry to promote public access to clinical trials, yet pharmaceutical outfits are unwilling to post sensitive proprietary clinical trial information on the Internet due to competitive or security concerns. An estimated 30% of the ongoing Phase II/III clinical trials ongoing are proprietary for pharmaceutical companies, with 10% of the trials completely confidential, 10% of the trials having confidential inclusion/exclusion criteria, and 10% having confidential site locations. Each pharmaceutical site thus posts only a small percentage of all clinical trials available, often leaving the patient or clinician to perform an exhaustive and often futile search. Patients and clinicians with limited resources or time constraints would hesitate to undertake such searches, particularly given the incomplete offerings at many sites.

Summary

In an embodiment, a system for recruiting a patient into a clinical trial comprises a patient interface; a set of patient-specific data, collected from the patient through the patient interface; a set of trial-specific criteria corresponding to the clinical trial; a content interface; a set of disease-specific data, collected from a disease expert through the content interface; and instructions for matching, including instructions for coupling the set of patient-specific data to the disease-specific data and producing a set of patient-disease characteristics, and instructions for coupling the set of patient-disease characteristics to the set of trial-specific criteria and determining whether a match exists between the patient and the clinical trial.

In an embodiment, the patient interface comprises an HTML-encoded web page.

In an embodiment, a system for recruiting a patient into a clinical trial further comprises a patient database, including the patient-specific data.

In an embodiment, a system for recruiting a patient into a clinical trial further comprises a clinical trial database, including the set of trial-specific criteria.

In an embodiment, a system for recruiting a patient into a clinical trial further comprises a disease database, including the set of disease-specific data.

In an embodiment, the patient-specific data, the disease-specific data, the trial-specific criteria, the instructions for matching, and the instructions for coupling are stored in a server.

In an embodiment, the patient interface is adapted for transmission over a network to a remote location.

In an embodiment, the content interface is adapted for transmission over a network to a remote location.

In an embodiment, the patient interface includes a series of questions.

In an embodiment, a system for recruiting a patient into a clinical trial further comprises instructions for coupling at least a portion of the patient-specific data to the clinical trial.

In an embodiment, a system for recruiting a patient into a clinical trial further comprises instructions for coupling a set of trial contact information to the patient.

In an embodiment, the patient-specific data comprises at least one of patient contact information, disease of concern, demographic data, drug classes of interest, prior therapies, specific drugs of interest, years since diagnosis, stage of disease, phase of clinical trial, and concomitant diseases.

In an embodiment, a system for recruiting a patient into a clinical trial comprises a patient database, residing on a server and including a set of patient-specific data; a criteria interface coupled to the server over a network; a set of clinical trial criteria corresponding to the clinical trial and collected through the criteria interface; and instructions for comparing the set of clinical trial criteria to the set of patient-specific data to determine whether a match exists between the patient and the clinical trial.

In an embodiment, a method for recruiting a patient into a clinical trial comprises serving a content interface by a server to a first remote location over a network; receiving a set of

disease-specific data from the content interface over the network, the set of disease-specific data collected from a disease expert through the content interface; serving a patient interface by the server to a second remote location over the network; receiving a set of patient-specific data from the patient interface over the network, the set of patient-specific data collected from the patient through the patient interface; filtering the set of patient-specific data in comparison to the set of disease-specific data to generate a set of patient-disease characteristics; comparing the set of patient-disease characteristics to a set of trial-specific criteria corresponding to the clinical trial; and determining whether a match exists between the patient and the clinical trial.

In an embodiment, a method for recruiting a patient into a clinical trial comprises compiling a patient database including a set of patient-specific data; storing the database on a server; serving a criteria interface from the server to a remote location over a network; receiving a set of clinical trial criteria corresponding to the clinical trial from the criteria interface; and comparing the set of clinical trial criteria to the set of patient-specific data to determine whether a match exists between the patient and the clinical trial.

In an embodiment, a computer program product, disposed on a computer readable medium for recruiting a patient into a clinical trial, comprises instructions for causing a processor to serve a content interface to a first remote location over a network; receive a set of disease-specific data from the content interface over the network, the set of disease-specific data collected from a disease expert through the content interface; serve a patient interface by the server to a second remote location over the network; receive a set of patient-specific data from the patient interface over the network, the set of patient-specific data collected from the patient through the patient interface; filter the set of patient-specific data in comparison to the set of disease-specific data to generate a set of patient-disease characteristics; compare the set of patient-disease characteristics to a set of trial-specific criteria corresponding to the clinical trial; and determine whether a match exists between the patient and the clinical trial.

In an embodiment, a method of recruiting a patient into a clinical trial comprises receiving patient-specific data from a remote network device at a server; accessing criteria of more than one clinical trial at the server; and determining one or more clinical trials having criteria satisfied by the patient-specific data.

In an embodiment, a server system for recruiting a patient into a clinical trial comprises sets of criteria corresponding to a different clinical trial; instructions for receiving patient

specific data from a remote network device; and instructions for determining one or more clinical trials having criteria satisfied by the patient specific data.

Brief Description of the Figures

FIG. 1 depicts a flowchart of a process for a patient attempting to match to a clinical trial.

FIG. 2 depicts a flowchart of a process for recruiting a patient into a clinical trial.

FIG. 3 depicts exemplary disease information.

FIGs. 4-6 depict exemplary questions to be answered by a patient.

FIG. 7 depicts exemplary trial match results.

FIG. 8 depicts an exemplary trial-specific question to be answered by a patient.

FIGs. 9-10 depict exemplary trial details.

FIG. 11 depicts an exemplary registration form for a user of the system to complete.

FIG. 12 depicts an exemplary patient data form for a user of the system to complete.

FIG. 13 depicts exemplary trial contact information.

FIG. 14 depicts a flowchart of an expert providing content for a recruiting system.

FIG. 15 depicts an exemplary content interface.

FIG. 16 depicts an exemplary disease interface.

FIG. 17 depicts an exemplary questionnaire builder.

FIG. 18 depicts an exemplary type selector.

FIG. 19 depicts an exemplary option count selector.

FIG. 20 depicts an exemplary question editor.

FIGs. 21-22 depict an exemplary trial association interface.

FIG. 23 depicts an exemplary criterion interface.

FIG. 24 depicts an exemplary trial-specific question interface.

FIG. 25 depicts an exemplary test interface.

FIG. 25A depicts exemplary test results.

FIGs. 26-27 depict exemplary questions to be answered by a patient.

FIG. 28 depicts exemplary match results.

FIG. 29 depicts an exemplary network architecture.

FIG. 30 depicts exemplary secure data flow.

Detailed Description

Described herein are techniques that can facilitate the matching of public and clinician interest in novel therapies with a comprehensive, secure database of public and private clinical trials to promote patient recruitment.

In an embodiment, the present disclosure describes techniques that can facilitate clinical trial recruitment using a network. In particular, the disclosure describes an approach for accelerating clinical trial recruitment by matching patient data submitted over the Internet to server-side maintained databases of public and private clinical trials in a secure manner so that patient information and proprietary clinical trial information are not compromised.

The system and method are implemented in part by a matching procedure, a security application and protocol, and patient and public and private clinical trial databases. The present disclosure also contemplates experimental treatment content review and analysis by experts to promote patient and clinician understanding.

In an embodiment, the patient, or clinician on behalf of the patient, inputs information including disease of concern, basic demographic data, drug classes of interest, prior therapies, specific drugs of interest, years since diagnosis, stage of disease, phase of clinical trial, other known diseases or infections, and various physiological, biochemical, and pathological parameters applicable to the disease of concern into the patient interface. The patient is presented different "levels" of questions and can answer as many as he/she feels comfortable. Once the patient-specific data is submitted, the server requests a match of the patient data to a clinical trials database maintained in the system. The rules-based matching algorithm compares a patient's eligibility criteria to the public and private trials in the database.

In another embodiment, the recruiting system uses security protocols to ensure that private data is kept confidential and to sanitize the information passed on to the client system.

The security application layer of the network monitors all protocols that are sent back and forth to the databases and allows the components of the system to remain autonomous. The security application may send only the data necessary for trial matching, a patient's eligibility criteria, to the trials database. Private trial data is not accessible via the web, while public trial data is displayed.

In yet another embodiment, pharmaceutical companies can post trial data or trial-specific criteria in the recruitment system to facilitate trial recruitment. The system may serve as an independent third-party hub for proprietary trial data. As a third party, the systems facilitates a marketplace that is structurally impossible for pharmaceutical companies, contract research organizations (CROs) and individual health portals to build. The system offers the necessary components of a trials marketplace: comprehensiveness, lack of bias (e.g., no 'selling' of particular trials), and transparency of market operation.

In another embodiment, pharmaceutical company can access the patient database to pre-enroll patients into clinical trials. Access to the patient database will accelerate patient recruitment and enhance the probability of attaining an appropriate patient population for a specific trial. As patients register through the patient interface, a database of patients who are interested in entering clinical trials is populated, eventually allowing new trials to be more fully enrolled prior to initiation.

The recruitment system may include a secure database system that matches patients with appropriate clinical trials while keeping proprietary trial information hidden.

In one practice, to match to a clinical trial in the trial database, patients and health professionals submit information to the system using a web-based patient interface. In an embodiment, the server generates Hyper-Text Markup Language (HTML) code or code in a similar language such as XML or GML to display the patient interface on a web page and to receive the patient-specific data submitted from a web page. Patients may enter information including contact information, disease of concern, basic demographic data, drug classes of interest, prior therapies, specific drugs of interest, years since diagnosis, stage of disease, phase of clinical trial, other known diseases or infections, and various physiological, biochemical, and pathological parameters applicable to the disease of concern. The patient may answer as many questions on the clinical trials questionnaire as he/she feels comfortable but answering more questions may result in better targeted trial matches.

Once a patient submits at least a portion of the patient-specific data, the server requests a match of the patient data to public and private clinical trials in the database. In one embodiment, the matching algorithm used by the system is rules-based. Upon entry of a new clinical trial into the system, the trial site coordinator or pharmaceutical company can determine the desired accuracy of patient matches. The rules-based matching system allows trial site coordinators and pharmaceutical companies to control the accuracy of patient matches, giving them great flexibility in matching to a desired patient pool. The rules-based system allows some trial sites to accept only patients that match 100% of the trial-specific criteria, while other trial sites can remain more lenient and require a lower matching percentage. A "match" exists for a trial if the patient-specific data submitted successfully passes enough of a trial's eligibility criteria to meet the specified percentage.

In an embodiment, the patient-specific data questions are organized by levels and presented to the patients through the patient interface on a level-by-level basis to maintain a user-friendly environment. The first level of questions may serve as an initial screening where patients are asked to submit basic information about their age, gender, and disease of concern. As a patient proceeds with the process and progresses to other levels in the patient interface, the questions become more detail-orientated and disease-specific.

In an embodiment, the match data may pass through a multi-tiered security layer and protocol to sanitize the information passed on to the client system. For non-proprietary trials, details such as contact information (i.e., name, phone number, and email address), trial description, trial location, drugs being tested, and eligibility criteria are displayed. For proprietary trials, unless otherwise specified, only trial contact information is displayed. All confidential proprietary trial details are hidden. Once the clinical trial data is sanitized by the security layer and protocol, the match results are sent to the server. The server formats the results for reporting to the patient. In an embodiment, the server generates HTML code to display the results on a web page.

In an embodiment, the proprietary trial and patient information is protected from unauthorized access. The secure database system protects sensitive pharmaceutical information (e.g., trial site locations, drugs in development, and trial eligibility criteria) while allowing trials to be matched to appropriate patients. The database system includes safeguards from hacking and spoofing while allowing pharmaceutical companies to alter the level of information

disclosure based upon accrual need. This is accomplished by using security protocols utilizing fine grain access control, highly redundant firewall/security systems, off-line storage of the most sensitive information as well as traditional safeguards such as 128-bit Secure Socket Layer ("SSL") encryption, unique identifiers, maximum number of requests per user per hour, and so forth. Patient information is also protected in this controlled environment, and will only be released to specifically designated partners with the patients' active consent.

In an embodiment, security measures that may be taken to ensure secure access to the databases include multi-tiered architecture; multiple firewalls; security reinforcement at the database level; off-line loading process for private trial data; fine-grained access control; and SSL encryption.

To match to a clinical trial in the trial database, a disease expert submits a set of disease-specific data via the content interface. A set of questions based upon the disease-specific data is presented to patients and health professionals via the patient interface. The patients and health professionals provide patient-specific data to the system in the form of responses to the questions. The patient-specific data is compared to the disease-specific data to determine a set of patient-disease characteristics. These characteristics are then compared to clinical trial eligibility criteria, and the existence of a match determined.

In an embodiment, the questions presented via the patient interface are organized by levels and presented to the patients on a level-by-level basis. The level-based approach to the questionnaire enables patients to filter trials gradually without being overwhelmed by an extensive list of trial-specific questions.

In an embodiment, patients have access to experimental treatment content created by experts. This content is made available through the patient interface. In an embodiment, the experts include Harvard M.D. editors. The content is provided to assist patients with answering accurately as many questions as possible in order to receive well-targeted trial results.

The content and clinical trials made available through the patient interface may focus on the following and other diseases: AIDS/HIV; Allergic Disorders; Alzheimer's Disease; Anxiety Disorders; Asthma; Bipolar Disorder; Bladder Disorders; Brain Tumors; Breast Cancer; Chronic Obstructive Pulmonary Disease; Chronic Pain; Colon Cancer; Congestive Heart Failure; Coronary Heart Disease; Crohn's Disease; Cystic Fibrosis; Depression; Diabetes; Ear, Nose, & Throat Disorders; End Stage Renal Disease; Endometriosis; Epilepsy; Fertility Treatments; Foot

Disorders; Gastrointestinal Disorders; Glaucoma; Hepatitis C; High Blood Pressure; High Cholesterol; HIV; Hodgkin's Disease; Hypertension; Incontinence; Infertility; Inflammatory Bowel Disease; Leukemia; Acute Lymphoid Leukemia; Acute Myeloid Leukemia; Chronic Lymphoid Leukemia; Chronic Myeloid Leukemia; Lung Cancer; Lupus; Lymphoma; Non-Hodgkin's Lymphoma; Menopause; Migraines; Multiple Sclerosis; Neuropathy; Obesity; Oral Disorders; Osteoarthritis; Osteoporosis; Ovarian Cancer; Pancreatic Cancer; Parkinson's Disease; Prostate Cancer; Psoriasis; Recurrent Pregnancy Loss; Reproductive Conditions; Rheumatoid Arthritis; Schizophrenia; Sexual Dysfunction; Sickle Cell Anemia; Skin Cancer; Skin Disorders; Sleep Disorders; Spinal Cord Injury; Stroke; Ulcerative Colitis; Uterine Fibroids; and Vascular Disorders.

A number of non-limiting examples will now be presented to illustrate more fully several aspects of the foregoing subject matter.

FIG. 1 depicts a flowchart of an embodiment in which a patient seeks to find matches to clinical trials for lung cancer therapies. In an embodiment, the patient connects to the patient interface **10** and requests disease information **12** specific for a certain disease or disease class. In an embodiment, a server (not shown) serves the interface **10** in the form of an HTML-encoded web page to a remote client (not shown). The patient may then elect to search for matching trials. The server then serves an initial set of questions **14** to collect, e.g., demographic data about the patient and the disease of interest to the patient.

After answers are submitted by the patient interface **10** to the server, the server serves a second set of questions **18** which address more specific detail than did the initial set of questions **14**. Questions included among the second set **18** may request information including drug classes of interest, prior therapies, specific drugs of interest, years since diagnosis, stage of disease, phase of clinical trial, other known diseases or infections, and various physiological, biochemical, and pathological parameters applicable to the disease of concern, in addition to other information. The answers to these questions are submitted by the interface **10** to the server.

The server then compares the responses to the first set of questions **14** and the second set of questions **18** to a set of criteria for a given clinical trial. If a match exists, then the trial is included in a set of match results **20**. If a patient is interested in pursuing a particular trial listed among the match results **20**, the server will then serve a set of trial-specific questions **22**, if any exist for the trial. The answers to the trial-specific questions **22** will be compared to the trial-

specific criteria to determine whether a match still exists. If it does, then the server will serve a set of trial details **24**. If the patient wishes to learn how to enroll in the trial, the patient completes a registration form **28** and a patient data form **30**. The server then serves trial contact information **32** to the patient.

In an embodiment, the server may perform a comparison of the patient answers to the set of criteria for a given clinical trial at any time. For example, a comparison may be performed between the responses to only the first set of questions **14** and the trial criteria.

FIG. 2 depicts another embodiment, in which a first level of questions **1** in the patient interface serves as an initial screening where patients are asked to submit basic information, e.g., about their age, gender, and disease of concern. As a patient proceeds with the process and progresses to other levels, the questions become more detail-orientated and disease-specific.

The questions presented in a second level **2** of the questionnaire are determined by the patient's response in level one. The number of trial matches **5** may be displayed. At any point, if a patient matches a small number of trials, the patient has the option to view the match results **9**. As the patient progresses with the process, the level 3 questions **3** are dynamically generated and, thus, are specific to the remaining potential trial matches. Finally, in level 4, the patient is presented with any unanswered questions **4** applicable to a selected trial's eligibility criteria, ensuring that the patient fully meets a trial's eligibility. Once match results **9** have been displayed, trial contact information **8** may be viewed.

In an embodiment, one or more levels of questions may be omitted. For example, the system may be configured so that all data necessary to test for the existence of a match is collected from the first level of questions. In another embodiment, the set of patient-specific data generated from answers to level one questions may be sufficient to meet or exceed the specified matching percentage for a given trial; in such a circumstance, the remainder of the questionnaire may be discarded and the match results reported immediately to the patient.

FIG. 3 depicts one embodiment of disease information **12** when the patient interface **10** comprises a set of web pages. Disease information **12** may include information about a disease of interest **302**, an expert **304** providing the content, background material **308**, therapy information **310**, such as information on, e.g., prevention therapy, combination therapy, pre-surgical and post-surgical therapy, chemotherapy before, during, and after radiation therapy, and

other therapeutic modalities known to one of ordinary skill in the art. Disease information **12** may also provide means for initiating a trial search **312**.

FIG. 4 depicts one embodiment of the first set of questions **14**. Questions may include, e.g., date of birth **402**, geographic location and preferences **404**, diagnosis **408**, and type and stage (not shown).

FIGs. 5 and 6 depict one embodiment of the second set of questions **18**. Questions may include, e.g., number of prior therapy regimens **502**, drug therapies undergone **504**, other therapy modalities undergone **508**, concomitant illnesses **602**, gender **604**, participation in clinical trials **608**, and other specific questions regarding, e.g., duration of diagnosis, organ involvement, family history, exacerbating conditions, and any other questions that expert **304** deems relevant.

FIG. 7 depicts an embodiment of match results **20**. A trial match **702** may include a series of trial sites **704a**, **704b**, and **704c**. The match results **20** may provide means for selecting a trial **708**.

FIG. 8 depicts an embodiment of a set of trial-specific questions **22**. A trial specific question **802** may be a very specific question, the answer to which alone may determine whether a patient matches to a trial.

FIGs. 9 and 10 depict an embodiment of a set of trial details **24**. The trial details **24** may include information concerning the location **902**, the purpose **904**, a detailed description **908**, eligibility criteria, trial source **1002**, data on drugs used in the trial, and other details known to be relevant by one of ordinary skill in the art. The trial details **24** may include means for requesting enrollment information **1004**.

FIG. 11 depicts an embodiment of registration form **28**, which may request, e.g., login data **1102**, contact data **1104**, and verification data **1108**.

FIG. 12 depicts an embodiment of patient data form **30**, which may request, e.g., non-unique identifying data **1202**.

FIG. 13 depicts an embodiment of trial contact information **32**, which may include trial title **1302**, trial sponsor **1304**, trial location **1308**, and trial contact entity **1310**.

FIG. 14 depicts a flowchart of an embodiment in which an expert provides content for questions through a content interface **34**. The server serves the content interface **34** to an expert, such as expert **304**. The expert selects a disease for which content is to be provided, and the server serves a disease interface **36.** From disease interface **36**, expert **304** may modify disease

information **12** and may add or modify questions for first set **14**, second set **18**, and for trial-specific questions **22**.

If expert **304** elects to add a new question, server serves a questionnaire builder **38**. Builder **38** includes a question type selector **40**, option count selector **42**, and question editor **44**. Once expert **304** has created a new question, the question is then associated with a trial through the trial association interface **48**. The server then serves a criterion interface **50** to permit expert **304** to specify whether a question constitutes an inclusion or exclusion criteria for the trial and what the answer should be to meet that criterion. Expert **304** may optionally add a trial-specific question using a trial-specific question interface **52.** Expert **304** may verify that the question is correctly associated with the trial through a test interface **54**.

FIG. 15 depicts one embodiment of content interface **34**. It may include an option to select a disease of interest **1502.**

FIG. 16 depicts one embodiment of disease interface **36**. It may include a disease information editor link **1602**, a questionnaire builder link **1604**, and a test interface link **1608.**

FIG. 17 depicts one embodiment of questionnaire builder **38**. Builder **38** may include an add question link **1702**, a reorder questions link **1704**, and an edit question link **1708.**

FIG. 18 depicts one embodiment of type selector **40**. It may include a list of question types **1802**.

FIG. 19 depicts one embodiment of option count selector **42**. Selector **42** may include a list of option counts **1902**.

FIG. 20 depicts one embodiment of question editor **44**. It may include a prompt **2002** to provide question text and prompts **2004** to provide answer texts. The format of prompts **2004** is determined by the options specified by expert **304** through the type selector **40** and option count selector **42**.

FIGs. 21 and 22 depict one embodiment of trial association interface **48**, which may include a list **2102** of trials relating to the selected disease and an action selector **2104**. The action selector has a list of actions including, e.g., to edit trial data, add a trial-specific question to the trial, and to associate the new question with the trial. A set of fields **2202** may be provided by which trial data may be edited.

FIG. 23 depicts one embodiment of criterion interface **50**. The criterion interface **50** includes the title **2302** of the selected trial and the first set **14** and second set **18** of questions.

Each question **2308** has an option indicator **2304** to permit the expert **304** to indicate whether the question is relevant for the selected trial. If a question is marked as relevant, then the patient's response to the question will be included in the comparison between the question answers and trial criteria. Expert **304** may indicate whether question **2308** is an inclusion criterion or exclusion criterion for the selected trial by choosing accordingly with a criterion selector **2310**. Expert **304** may then indicate which of answers **2312** must be chosen by the patient in order to fulfill the criterion.

FIG. 24 depicts trial-specific question interface **52**, which may include a question type selector **40**, option count selector **42**, and question editor **44**, as for question builder **38**. It may include a prompt **2402** for entering question text and a default selector **2404** for, e.g. a yes-or-no type question.

FIG. 25 depicts test interface **54**, which includes a mock-up version **2502** of a question for expert **304** to answer.

FIG. 25A depicts the results of comparing the test responses against the trial-specific criteria. For each trial identified by trial title **2504**, a set of answer matches **2508** is provided and a match percentage **2510** reported.

With reference to FIG. 26, the level 1 questions can be used as an initial filter for patients. Patients enter information including disease of concern, age, and gender. FIG. 26 illustrates one embodiment of the patient interface displaying a portion **2602** of the level 1 questions that may be presented for Breast Cancer.

With reference to FIG. 27, the level 2 questions can be determined from the answers given in level 1. These questions are more detail-oriented and disease-specific. Patients may enter information including drug classes of interest, prior therapies, specific drugs of interest, years since diagnosis, stage of disease, phase of clinical trial, other known diseases or infections, and various physiological, biochemical, and pathological parameters applicable to the disease of concern. FIG. 27 illustrates one embodiment of the patient interface displaying a portion **2702** of the level 2 questions that may be presented for Breast Cancer.

In an embodiment, once the match results are sanitized by the security application, the appropriate match results are displayed to the patient. For non-proprietary trials, details such as contact information (i.e., name, phone number, and email address), trial description, trial location, drugs being tested, and eligibility criteria are displayed. For proprietary trials, unless

otherwise specified, patients are only shown the trial contact information. All confidential proprietary trial details are hidden and are not accessible via the web. FIG. 28 illustrates one embodiment of the patient interface displaying a portion **2802** of the match results that may be presented for Breast Cancer.

An embodiment comprises a security application layer to allow patients to be matched with appropriate clinical trials while ensuring proprietary trial information is hidden. A secure database system protects sensitive pharmaceutical information (e.g., trial site locations, drugs in development, and trial eligibility criteria) while allowing trials to be matched to appropriate patients.

With reference to FIG. 29, a secure network architecture may include a network **2902**, an external firewall **2904,** a plurality of web application servers **2908**, a plurality of security applications **2910**, an internal firewall **2912**, a public database **2914**, and a private database **2918.** The equipment making up these elements may include Sun Microsystems enterprise servers; Cisco firewalls, switches and routers; Oracle 8*i* Enterprise database server; Cold Fusion web application servers; and an Apache web server.

Although it is extremely unlikely that the public servers **2908** ("WWW") will be compromised, the architecture is designed to minimize the damage that can occur in the unlikely event of a breach. The architecture features security applications, multi-tiered arrangement, multiple firewalls, security reinforcement at the database level, off-line loading process for private trial data, fine-grained access control, and Secure Socket Layer encryption.

In an embodiment, a security application **2910** allows for extremely fine-grained control over the data escaping the database and provides an extra layer of network security that a hacker must penetrate before gaining access to valuable trial and patient data. Login alerts on the security application are set up to alert a system administrator to a penetration as it happens. The alerts, in the form of e.g. a page, will allow the administrator to immediately detect the occurrence of unauthorized shell start-ups.

The security application **2910** can be database-based. A small data-caching database can be set up on the security application server. This database can be pushed, using rules programmed and contained on the database, with only the sanitized data that is allowed onto the web page.

In an embodiment, the network architecture is multi-tiered to ensure that private trial and patient data is completely inaccessible from the World Wide Web. All requests submitted to the databases must successfully pass through both the web application server layer **2908** and the security application layer **2910**. In addition, two distinct firewalls **2904, 2912** provide additional tiers to further separate private data from the Internet and ensure the system cannot be penetrated.

In an embodiment, multiple firewalls **2904, 2912** are provided. A firewall can control network services both in and out of a network. A perimeter firewall provides several types of protection, including: limiting public users to accepted network traffic; controlling Virtual Private Network (VPN) services from authorized client machines (i.e. experts' machines within an office); and protecting the data center network from many Denial of Service attacks.

The network architecture, as depicted in FIG. 29, allows for a firewall **2912** to be placed in proximity to the private database **2918**. Firewall **2912** can protect the private database **2918** from unauthorized access from machines trusted by the perimeter firewall. All other machines within proximity to the private database **2918** and machines connected to the data center network via VPN classify as machines trusted by the primary firewall **2904**. The secondary firewall **2912** will control which content managers have access to the private data and which data center machines can request private data. The firewall automatically flags inappropriate requests from unauthorized machines.

In an embodiment, data leaving the database is carefully monitored to ensure that valuable data cannot escape. This restrictive data security policy can frustrate most attempts to obtain private data without authorization. There are two different security levels in the database setup: first, data that is read/write accessible directly from the web; second, highly confidential data is stored separately from the web-accessible data. A very strict security layer allows only specific, pre-determined confidential trial information to pass out of the database. All of the medical content and patient data can also be kept behind the security layer.

In an embodiment, a sophisticated matching algorithm compares the patient's data to the clinical trial eligibility data. Matching patient characteristics to both private and public clinical trial eligibility conditions should occur in a secure manner. The bulk of proprietary clinical data should not be passed over to the web side. Instead, only very specific contact information for matching clinical trials should be passed.

In an embodiment, the raw proprietary clinical trial feed received from clinical trial conductors may be held on yet another machine entirely. For maximum security, this machine may not even be on a network. From this "off-line" machine, a first pass of data cleaning and sanitization can be done. Then, data can be loaded into the proprietary database via a "sneaker-net" (e.g. tape, floppy, Zip disk, or CD-Rom), further minimizing the chances of that highly valuable data escaping the organization.

In an embodiment, data scavenging can be thwarted by a harm-reduction security layer on the database itself. The security application protocol is designed to accept requests from particular machines (e.g., the web server wants a patient to clinical trial match) and validate those requests against a short list of acceptable choices (e.g., the web server is asking for one patient's match results, rather than the entire clinical trial data set). Then, the application passes this validated request on to the appropriate database (public, private or both) and assembles an appropriate answer for the web server's question.

In an embodiment, the system may throttle the amount and type of data available to the web application. Without row-level security, the web application might otherwise have to be granted full select (and/or insert, update and delete) access to the database. The web application itself should guarantee that each customer is his or herself, and the web application is responsible for asking the database for only the appropriate customer rows. If the web application is compromised or subverted in a manner that allowed the privileged web application entity to ask for the entire customer table, confidential customer data could be scavenged in its entirety.

Fortunately, row-level security allows the server to enforce throttling rules about how much data the web application can ask for at any one time. For patient data access, the database may allow only a single patient row to be returned by any one query. In order for the malicious competitor to scavenge all the valuable data, they would have to call similar URLs repeatedly, giving the web application security and abuse procedures time to identify the single IP-address querying for each customer record in turn, and shut out the offender. Not only does this policy gain the administrators' valuable time by preventing the wholesale harvesting of data, it also requires the hacker to know individual-specific login names to retrieve any data.

In an embodiment, the server gathers sensitive information about patients and matches against ongoing clinical trials. Private patient data may travel over the public Internet. To

ensure patient confidentiality, the web session can be encrypted via 128-bit Secure Socket Layer (SSL) enabled web servers and browsers.

In an embodiment, depicted in FIG. 30, the flow of data to and from the security application is handled as follows:

1. Patient **3002** submits patient-specific data
2. Web server (not shown) requests a trial match
3. Security application **3010** asks patient database for patient data
4. Patient data sent to security application **3010**
5. Security application **3010** asks trials database **3004** for a trial match
6. Match results returned to the security application **3010**
7. Match results sent to Web server
8. HTML generated
9. Match results displayed on the patient's PC

The security application layer **3010** of the network allows the components of the system to remain autonomous. The trials database **3004** is maintained separately from the patient database **3008**, and the security application **3010** monitors all protocols that are send back and forth to the databases **3004, 3008**. The security application **3010** sends only the data necessary for trial matching, a patient's eligibility criteria, to the trials database **3004**. Patient demographic data (e.g. name, address, and email) is not used in the matching algorithm.

In an embodiment, the security application layer also sanitizes the information passed on to the client system. For non-proprietary trials, details such as contact information (i.e., name, phone number, and email address), trial description, trial location, drugs being tested, and eligibility criteria are displayed. For proprietary trials, unless otherwise specified, the security protocols ensure that all confidential, proprietary trial details are hidden. Only trial contact information is displayed on the web.

An embodiment includes an independent database where pharmaceutical companies can post trials in order to facilitate trial recruitment. The system can serve as an independent third-party hub for proprietary trial data. As a third party, the system can create a marketplace that is structurally impossible for pharmaceutical companies, contract research organizations (CROs) and individual health portals to build. The system offers the necessary components of a trials

marketplace: comprehensiveness, lack of bias (e.g., no 'selling' of particular trials), and transparency of market operation.

Pharmaceutical companies can submit trial data to the Clinical Trial Patient Recruitment system by several methods, including: uploading a batch of trial data is into the trials database; or submitting trials one-by-one via a web interface.

Upon submission of a trial, the trial is associated with the desired matching percentage for use in the rules-based matching algorithm. The matching percentage can be site-specific or centralized. Also, upon submission, the appropriate questions are associated with the trial's eligibility criteria.

An embodiment includes a patient database that pharmaceutical companies can access to accelerate patient recruitment. Such a patient database can accelerate patient recruitment with an enhanced probability of attaining an appropriate patient population. A pharmaceutical company can access the patient database to pre-enroll patients into clinical trials. Access to the patient database can accelerate patient recruitment and enhance the probability of attaining an appropriate patient population for a specific trial.

In an embodiment, patients have the option of voluntarily sharing their data with pharmaceutical companies in order to receive information about upcoming trials and relevant treatments. As patients register with the system, they may be added to a database of patients who are interested in entering clinical trials. This facilitates fuller enrollment in clinical trials prior to initiation. This database may become increasingly important as the fields of combinatorial chemistry and genomics spawn thousands of new drug candidates in the near future.

In an embodiment, physicians may access the system to identify trials that may be of interest to their patient or to identify trials that might benefit from opening a new trial location in the vicinity of the physician's office.

In an embodiment, clinical trials may transmit back to the server data concerning patients that have been enrolled in the trial as a result of having matched using the techniques described herein.

In an embodiment, the server can notify patients when new clinical trials become available to which the patients are likely to match, as determined by patient-specific data retained in the patient database.

The techniques described herein are not limited to any particular hardware or software configuration; they may find applicability in any computing or processing environment. The techniques may be implemented in hardware or software, or a combination of the two. Preferably, the techniques are implemented in computer programs executing on programmable computers that each include a processor, a storage medium readable by the processor (including volatile and non-volatile memory and/or storage elements), at least one input device, and one or more output devices.

Each program is preferably implemented in high level procedural or object oriented programming language to communicate with a computer system. However, the programs can be implemented in assembly or machine language, if desired. In any case the language may be compiled or interpreted language.

Each such computer program is preferably stored on a storage medium or device (e.g., CD-ROM, hard disk, or magnetic disk) that is readable by a general or special purpose programmable computer for configuring and operating the computer when the storage medium or device is read by the computer to perform the procedures described herein. The system may also be considered to be implemented as a computer-readable storage medium, configured with a computer program, where the storage medium so configured causes a computer to operate in a specific and predefined manner.

Various alternative embodiments are envisioned and within the scope of the claims. While the subject matter has been particularly shown and described with reference to a number of embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the subject matter.

Having disclosed the foregoing subject matter and embodiments thereof, what is claimed as new and secured by Letters Patent is: